



## REMARKS

**Rejection under 35 U.S.C. § 103**

In the February 12, 2002 Advisory Action, the Office conceded that applicants' previous argument pertaining to the combination of Donnelly, et al. and the Johnson references was convincing. Specifically, the combination does not teach the generation of one polypeptide containing multiple domains. However, according to the Office,

"the instant claims can fairly be interpreted to encompass fusion proteins of the ORFs or fragments thereof."

The Office then cites a paragraph in the present specification wherein a "fusion protein" is referred to as polypeptides which can be present in any combination (see page 3 last paragraph). The Office then wrongly interprets this statement to mean that the claimed fusion proteins of the present invention do not require both the L- and E-ORFs.

Applicants vigorously disagree. The Office has overlooked statements made on the previous page of the specification, wherein it is explicitly stated that the fusion polypeptide comprises both a structural polypeptide and a non-transforming polypeptide. Thus, both a structural and non-transforming polypeptide have to be included in the fusion protein. Clearly, when applicants made reference to "any combination" in the specification, the statement must be read in the context of the previous paragraphs that explicitly set forth the different types of structural and non-transforming polypeptides. Thus, applicants clearly meant that any combination could include a choice of different L-ORFs combined with different E-ORFs.

It is clear and the Office agrees that the cited combination fails to establish a *prima facie* case of obviousness of applicants' claimed invention.

**Petition for Extension of Time/Fees Payable**

The applicants hereby petition for a one (1) month extension of time, extending the deadline for responding to the December 4, Office Action from March 4, 2002 to April 4, 2002. The entry of this petition results in a petition fee of \$55.00. A check in the amount of \$425.00 which includes the petition fee is submitted herewith. The U.S. Patent and Trademark Office is hereby authorized

to charge any additional amount necessary to the entry of this amendment, and to credit any excess payment, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

**CONCLUSION**

It is requested that the examination and prosecution of this application proceed on the basis of these amended claims 14 -61 and 65-66.

Respectfully submitted,



Marianne Fuierer  
Registration No. 39,983  
Attorney for Applicant

INTELLECTUAL PROPERTY/  
TECHNOLOGY LAW  
P.O. Box 14329  
Research Triangle Park, NC 27709  
Telephone: (919) 419-9350  
Fax: (919) 419-9354  
Attorney Ref: 4121-107

In response to the December 4, 2001 Office Action in the above-referenced patent application, the deadline for response to which has been extended by one (1) month to April 4, 2002 by the petition under 37 CFR 1.136 set out hereinafter, please amend the application as follows:

### In the Claims<sup>1</sup>

Please amend claims 14, 49, 50, 51, 52, 53, 61 and 65 to read as follows:

14. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides or fragments thereof are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

49. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the

<sup>1</sup> Applicants have provided a marked-up version of the amended claims 14, 49, 50, 51, 52, 53, 61 and 65 in Appendix A, and a clean set of all pending claims, amended to date, in Appendix B.

structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

50. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus peptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide, and the human papillomavirus of (a) and (b) is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

51. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

52. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an HPV16 or 18 L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

53. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by HPV16 or 18 L1-ORF; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of: E6-ORF and E7-ORF, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

65. (Twice Amended) A method for activating an immune system of a subject comprising administering to the subject an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to

1 37 10  
code for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a  
N-terminus of the non-transforming polypeptide.

## APPENDIX A

### In the Claims

Please amend claims 14, 49, 50, 51, 52, 53, 61 and 65 to read as follows:

14. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides or fragments thereof are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

49. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of [the] a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

50. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus peptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide, and the human papillomavirus of (a) and (b) is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

51. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

52. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an HPV16 or 18 L1-ORF or a fragment thereof; and



an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

53. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by HPV16 or 18 L1-ORF; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of: E6-ORF and E7-ORF, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

65. (Twice Amended) A method for activating an immune system of a subject comprising administering to the subject an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a [the] non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

**APPENDIX B**

14. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides or fragments thereof are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

15. The vector of claim 14 wherein the structural papillomavirus polypeptide is an HPV polypeptide.

16. The vector of claim 15 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

17. The vector of claim 14 wherein the early papillomavirus polypeptide is an HPV polypeptide.

18. The vector of claim 17 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

19. The vector of claim 14 wherein both the structural papillomavirus polypeptide and the early papillomavirus polypeptide are HPV polypeptides.

20. The vector of claim 19 wherein the HPV is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

21. The vector of claim 14 wherein the nucleotide sequence is under the control of a constitutive promoter.
22. The vector of claim 14 wherein the nucleotide sequence is under the control of an inducible promoter.
23. The vector of claim 14 wherein the nucleotide sequence is under the control of a tissue-specific promoter.
24. The vector of claim 14 wherein the nucleotide sequence is under the control of a tumor-specific promoter.
25. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by L1-ORF.
26. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by a fragment of L1-ORF.
27. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by L2-ORF.
28. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by a fragment of L2-ORF.
29. The vector of claim 14 wherein the structural papillomavirus polypeptide is encoded by HPV 16 L1 ORF.
30. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E1-ORF.
31. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E1-ORF.

32. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E2-ORF.
33. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E2-ORF.
34. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E4-ORF.
35. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E4-ORF.
36. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E5-ORF.
37. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E5-ORF.
38. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E6-ORF.
39. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E6-ORF.
40. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by E7-ORF.
41. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by a fragment of E7-ORF.
42. The vector of claim 14 wherein the early papillomavirus polypeptide is encoded by HPV 16 E6-ORF.

43. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by E6-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by L2-ORF or a fragment thereof.

44. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by HPV 16 E7-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

45. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by HPV 16 E6-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

46. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by HPV 16 E7-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by HPV 16 L2-ORF or a fragment thereof.

47. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by HPV 18 E6-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by HPV 18 L2-ORF or a fragment thereof.

48. The vector of claim 14 wherein:

the early papillomavirus polypeptide is encoded by HPV 18 E7-ORF or a fragment thereof; and  
structural papillomavirus polypeptide is encoded by HPV 18 L2-ORF or a fragment thereof.

49. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the

structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

50. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of L1-ORF and L2-ORF; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF and E7-ORF, wherein said early human papillomavirus peptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide, and the human papillomavirus of (a) and (b) is selected from the group consisting of HPV 16, HPV 18, HPV 33, HPV 35 and HPV 45.

51. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

52. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by an HPV16 or 18 L1-ORF or a fragment thereof; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early human papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

53. (Twice Amended) An adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural human papillomavirus polypeptide encoded by HPV16 or 18 L1-ORF; and

an early human papillomavirus polypeptide encoded by an HPV 16 or 18 open reading frame selected from the group consisting of: E6-ORF and E7-ORF, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

54. The vector of claim 53 wherein the ORFs of (a) and (b) are HPV 16 ORFs.

55. The vector of claim 53 wherein the ORFs of (a) and (b) are HPV 18 ORFs.

56. The vector of claim 53 wherein:

the ORFs of 53(a) and 53(b) are HPV 16 ORFs; and

the early human papillomavirus polypeptide is encoded by E6-ORF.

57. The vector of claim 53 wherein:

the ORFs of 53(a) and 53(b) are HPV 18 ORFs; and

the early human papillomavirus polypeptide is encoded by E6-ORF.

58. The vector of claim 53 wherein:

the ORFs of 53(a) and 53(b) are HPV 16 ORFs; and

the early human papillomavirus polypeptide is encoded by E7-ORF.

59. The vector of claim 53 wherein:

the ORFs of 53(a) and 53(b) are HPV 18 ORFs; and

the early human papillomavirus polypeptide is encoded by E7-ORF.

60. A vaccine composition comprising:

the vector of claim 14; and

an auxiliary agent.

61. The vaccine composition of claim 49 further comprising one or more immune system-activating agents.

65. (Twice Amended) A method for activating an immune system of a subject comprising administering to the subject an adeno-associated virus vector comprising a nucleotide sequence encoding a fusion polypeptide, the fusion polypeptide comprising:

a structural papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: L1-ORF, L2-ORF and fragments of any of the foregoing ORFs; and

an early papillomavirus polypeptide encoded by an open reading frame selected from the group consisting of: E1-ORF, E2-ORF, E4-ORF, E5-ORF, E6-ORF, E7-ORF and fragments of any of the foregoing ORFs, wherein said early papillomavirus polypeptides are non-transforming, and wherein the 3' end of the structural ORF is ligated to the 5' end of a non-transforming ORF to encode for the fusion polypeptide having a C-terminus of the structural polypeptide connected to a N-terminus of the non-transforming polypeptide.

66. The method of claim 65 wherein the fusion polypeptide is administered as a component of a vaccine composition.